

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of )  
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Robert T. Foster et al. ) Group Art Unit:  
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Application No.: ) Examiner:  
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Filed: November 14, 2001 )  
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For: METHOD OF USING DEUTERATED )  
CALCIUM CHANNEL BLOCKERS )

**PRELIMINARY AMENDMENT**

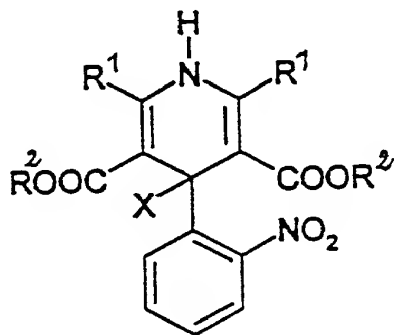
Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination of the above-referenced application, which is a continuation application of 09/558,325, please enter the following amendment.

Please cancel claims 1-28 and add claims 29-44 as follows:

29. A dihydropyridine compound wherein at least one of the hydrogen atoms is replaced with a deuterium atom, characterized in that said dihydropyridine compound is deuterated nifedipine having the formula

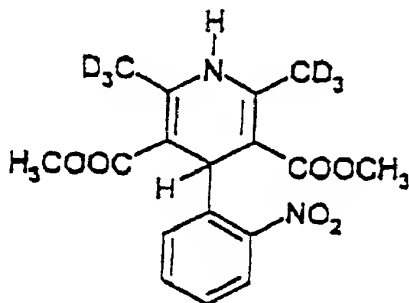


wherein:

$X=H$ ,  $R^1 = CH_3$  wherein each H-atom may be replaced by a D-atom, and  $R^2=CH_3$  wherein at most 5 out of the total 6H atoms may be replaced by a D atom, and wherein at least one of  $R^1$  and  $R^2$  together contains a D-atom.

30. The dihydropyridine of claim 29 wherein at least one of the methyl groups in the 2,6-position is  $CD_3$ .

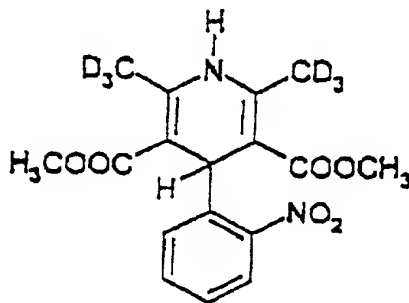
31. The dihydropyridine of claim 29 wherein  $X=H$ ,  $R^1=CD_3$  and  $R^2=CH_3$  of formula



32. A pharmaceutical composition for use as a medicament comprising one or more dihydropyridine compounds of claim 29 as the active ingredient and a pharmaceutically acceptable support.

33. The pharmaceutical composition of claim 32 wherein the dihydropyridine compounds are characterized in that at least one of the methyl groups in the 2,6-position is  $CD_3$ .

34. A pharmaceutical composition of claim 32 wherein  $X=H$ ,  $R^1=CD_3$  and  $R^2=CH_3$  of formula



35. A calcium channel blocking 1,4-dihydropyridine compound selected from nifedipine and nicardipine with an extended duration of action compared with a non-deuterated nifedipine and nicardipine, respectively, wherein one or more hydrogen atoms of one or both of the methyl groups in the 2 and 6 positions are replaced with a deuterium atom.
36. The dihydropyridine compound of claim 35 characterized in that all hydrogen atoms of the methyl groups in the 2 and 6 positions are replaced with deuterium atoms.
37. A method of extending the duration of action of a calcium channel blocking undeuterated 1,4-dihydropyridine compound selected from nifedipine and nicardipine whereby one or more hydrogen atoms of one or both of the methyl groups in the 2 and 6 positions are replaced with a deuterium atom.
38. The method of claim 37 wherein the dihydropyridine compound is characterized in that all hydrogen atoms of the methyl groups in the 2 and 6 positions are replaced with deuterium atoms.
39. A calcium channel blocking 1,4 dihydropyridine compound selected from nifedipine and nicardipine with an enhanced use dependency compared with a non-deuterated nifedipine and nicardipine, respectively, whereby one or more hydrogen atoms of one or both of the methyl groups in the 2 and 6 positions are replaced with a deuterium atom.
40. The dihydropyridine compound of claim 39 characterized in that all hydrogen atoms of the methyl groups in the 2 and 6 positions are replaced with deuterium atoms.

41. A method of enhancing the use dependency of a calcium channel blocking 1,4-dihydropyridine compound selected from nifedipine and nicardipine, compared with a non-deuterated nifedipine and nicardipine, respectively, whereby one or more hydrogen atoms of one or both of the methyl groups in the 2 and 6 positions are replaced with a deuterium atom.

42. The method of claim 41 wherein the dihydropyridine compound is characterized in that all hydrogen atoms of the methyl groups in the 2 and 6 positions are replaced with deuterium atoms.

43. A method of modifying the dose-response relationship of a calcium channel blocking 1,4-dihydropyridine compound selected from nifedipine and nicardipine, compared with a non-deuterated nifedipine and nicardipine, respectively, whereby one or more hydrogen atoms of one or both of the methyl groups in the 2 and 6 positions are replaced with a deuterium atom.

44. The method of claim 43 wherein the channel blocking 1,4-dihydropyridine compound is characterized in that all hydrogen atoms of the methyl groups in the 2 and 6 positions are replaced with deuterium atoms.

Respectfully submitted,  
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